Review article

Down syndrome in sub-Saharan Africa

Arnold L Christianson

Down syndrome (DS), which is now recognised as the commonest cause of congenital mental disability in developed countries,[1] was first described by Langdon Down in 1866.[2] However, not until 1955 did Luder and Musoke[3] recognise and describe the first black African children with DS. Before this, no less an authority than Jellife[4] had commented that "Mongolism occurs commonly in all ethnic groups, with the possible exception of people of African extraction amongst whom it would appear to be uncommon or even rare." In justifying his comment he noted his six year experience with African children in the southern Sudan and Nigeria during which time he saw no DS cases. He then proceeded to suggest that in view of the apparent rarity of DS in "unmixed African populations on the African continent", the fact that the condition was common in Jamaican children suggested that the causative factor must therefore be acquired from non-African, that is, white or Asiatic, sources.[4]

DS has beome one of the most researched and well documented genetic conditions. This volume of work up till 1980 comprised over 6000 papers with an even larger number of publications appearing in print since then.[5] However, to the best of the author's knowledge, to the present fewer than 25 papers have dealt, specifically or in passing, with DS in African populations south of the Sahara. It took until 1982 for Adeyokunnu[6] to lay to rest the myth of the rarity of DS in Africans. Since then, very little further research has been undertaken, possibly because of the emphasis in Africa on the eradication of malnutrition and infectious diseases, coupled with the continuing lack of awareness of the incidence of DS and difficulties inherent in the diagnosis of the condition in African neonates.

(J Med Genet 1996;33:89–92)

Key words: Down syndrome; sub-Saharan Africa.

Incidence and prevalence

After the first documentation of DS in African children by Luder and Musoke,[3] numerous attempts to study the incidence of DS in African populations gave contradictory results and floundered owing to incomplete ascertainment at birth, high mortality in infancy, and short periods of case collection.[3 6] The first reliable documentation of the incidence of DS was by Adeyokunnu[6] in 1982. This retrospective study

over nine years at the academic hospital, Ibadan, Nigeria, recorded an incidence of 1·16 per 1000 livebirths. It can be anticipated that the DS incidence reported in this series may have been lower than the true incidence owing to incomplete ascertainment of cases, but this was the first paper to document conclusively an incidence of DS in African newborns similar to other populations throughout the world.[6]

More recently, in three separate prospective studies in South Africa, the DS incidence in African newborns has been shown to be as high as, and in some circumstances higher, than that occurring in other populations. In 1995 Delport et al[7] documented an incidence of 1·33 per 1000 livebirths in a Pretoria urban academic hospital, and Venter et al[8] recorded a figure of 2·09 per 1000 livebirths in a rural hospital. Before this, Kromberg et al[9] in 1992 recorded an interim DS incidence of 1·67 per 1000 livebirths at an academic hospital in Johannesburg. In these three studies, 52%, 56%, and 55%, respectively, of the mothers of the DS infants were 35 years of age or older.[7–9] Subsequently the incidence of DS in the latter study[9] has been refined to 1·8 per 1000 livebirths for those infants born in Baragwanath Hospital, Johannesburg, and 1·2 per 1000 livebirths if the deliveries from the surrounding clinic maternity units were included (J G R Kromberg, personal communication.) The latter figures highlight the problem of ascertainment of cases in the South African studies and probably the Nigerian study. Owing to pressure on available beds, it is the policy in most South African maternity units to discharge all mothers and their infants within 24 hours of delivery if both are considered to be well. This policy, combined with the problems encountered in recognising the African DS neonate, heighten the likelihood of DS cases not being recognised during the infant's postnatal maternity unit admission. This is highlighted by figures from a study of 55 DS infants and children, 3 months of age and older, seen by the author. In only nine (16·4%) cases was the diagnosis of DS entertained during the patients' post delivery stay in hospital (A L Christianson, unpublished data).

To the present, the prevalence of DS in African populations is unknown. In a study on disability in children between 2 and 9 years of age at present being undertaken in a rural population in the Eastern Transvaal, South Africa, only two children with DS out of a total

Department of
Human Genetics,
Faculty of Medicine,
University of Pretoria,
PO Box 2034,
Pretoria 0001,
South Africa
A L Christianson

of 4168 screened have been recorded to date (J G R Kromberg, personal communication). Given the incidences of DS previously recorded, and the above minimum recorded prevalence of 1 in 2084 children, this would indicate a significant mortality of DS infants and children between birth and 2 years of age.

Clinical features and cytogenetics

Several authors have commented that it may be more difficult in routine clinical practice to diagnose DS in African infants and children than it is in other ethnic groups.[3 10 11] Mgone[12] and Christianson et al[11] documented the clinical features of African DS children and neonates and confirmed that, with the exception of minor variations, their phenotype was very similar to that documented in DS infants and children from other parts of the world. Despite this, in a study undertaken to identify the extent of the diagnostic difficulties, it was shown that one third of African newborns were incorrectly diagnosed by medical practitioners.[13]

In an effort to clarify the diagnostic problems encountered by medical practitioners, Christianson et al[11] compared the clinical features of African DS and normal neonates to those of white DS and normal neonates previously documented by Hall.[14] The results show a remarkable similarity in the musculoskeletal and central nervous system features of all four groups. When comparing the craniofacial features, reasons why DS may be less easily recognised in African DS neonates were identified. The typical flat facial profile and flat nasal bridge, commonly noted in both black and white DS newborns, occurred in 64% and 68% respectively of normal African newborns. Oblique palpebral fissures and epicanthic folds were similarly common in both groups of DS infants. Epicanthic folds were present in significantly more black than white normal newborns, and the situation was similar with oblique palpebral fissures, but the difference in their rates was not significant. Thus these features would possibly not initiate the same clinical concern when observed in African compared to white newborns. A protruding tongue and excess neck skin were significantly less frequent in black compared to white DS infants. The occurrence of a flat occiput/brachycephaly has also been noted to be less frequent in African children and only occurred in 30% of African neonates.[3 11]

These findings suggest that the clinical craniofacial features of African DS newborns approximate more closely to the craniofacial features of normal newborns than is the case between white DS and normal neonates, thus explaining the problems associated with clinical diagnosis in African neonates. This, in conjunction with the apparent lack of awareness of DS in this population and the very short periods spent by most African newborns in maternity units post delivery, provides an explanation for the underdiagnosis of DS in African neonates.[11]

Congenital heart disease, which presented in only 14% of the DS children described by Mgone,[12] was recorded in 32·5% of the neonates documented by Christianson et al.[11] However, in the series of 55 African DS infants and children 3 months of age and older, 14 (51·9%) of the 27 infants less than 1 year of age had congenital heart defects, compared to seven (25%) of the 28 DS children older than one year. Furthermore, six (42·9%) of the affected infants had concomitant congestive cardiac failure, as opposed to one (14·3%) of the seven DS children. This child was 13 months old. Only a single patient in this series had had corrective cardiac surgery (A L Christianson, unpublished data). These figures suggest that a significant proportion of the mortality of African DS infants and children previously alluded to is a consequence of congenital heart disease. This is compatible with the experience in developed countries, both past and present.[14 15]

Cytogenetic analyses of African DS patients have, in those studies reported, shown a pattern consistent with reports from elsewhere in the world. Combining the results of the three studies available, a total of 448 cases were reported, in which 429 (95·7%) were trisomy 21, translocations were found in 12(2·7%), and seven (1·6%) were mosaic DS.[6–8]

Maternal considerations

It has long been known that the risk of bearing an infant with DS increases with advancing maternal age. Adeyokunnu[6] reported that only 20·7% of the mothers in his series were 35 years of age or older (advanced maternal age or AMA), but noted that it was not possible to obtain accurate records of maternal ages for all deliveries, as the majority of mothers were ignorant of their correct ages. In the three South African studies, AMA was documented in 52%, 56·2%, and 55% respectively, of the mothers of DS infants.[7–9] In line with these figures, Christianson et al[16] noted 60% of the DS infants born in that study were the fourth or higher in the birth order, and Adeyokunnu[6] found this to be the situation in 76% of his cases.

Given the fact that most African mothers with DS infants were experienced mothers, it was therefore surprising to find that 82·9% of 35 mothers of DS neonates (80% of whom were 1 week or older) did not recognise that their infant's facial features were different from those of other infants, and 57·1% had not noted any other abnormality. Furthermore, 40% of all the mothers initially denied the diagnosis after full and careful counselling.[16] When undertaking this study, the authors also confirmed that DS was an unrecognised entity in the community and that there was no specific word for the condition in the vernacular.[13 16]

In a study of African DS mothers in Tanzania, Mgone[17] noted that their reproductive attitudes and behaviour remained unchanged following the birth of a DS child. Those mothers, however, who did not wish to have further children gave the reason as their advanced maternal age rather than their DS infant. This could be partly explained by parental lack of

awareness of DS, its aetiology, features, and prognosis, if it is assumed that a similar situation to the one described above[16] existed in Tanzania.

These findings raise the issues of prenatal counselling for African women of advanced maternal age and for those with a previous DS infant, selective termination of affected fetuses, and counselling of older mothers regarding the advantages of family planning. Are these services of benefit in a situation in which there is limited community knowledge of the major condition for which the counselling and management is being offered? Both the methods available for the prevention of DS, that is, those related to recurrence and occurrence (prenatal diagnosis and family planning), are thus potentially nullified by the high rate of maternal non-recognition of DS and the mothers' consequent unchanged reproductive behaviour.[16 17]

However, Kromberg *et al*[9] noted that 73% of African women with a DS child would have accepted prenatal diagnosis had it been offered to them, and 52% said they would have acted on the information provided and requested selective termination of pregnancy. This finding suggests that African women with knowledge and experience of children with DS, if offered prenatal diagnosis, would respond similarly to women in the same circumstances from other populations. This was confirmed in a prospective study of women attending the prenatal counselling clinic in Cape Town for counselling for AMA, an abnormal fetal ultrasound finding, or being at increased risk of a fetal anomaly. No significant differences were noted between the women of different ethnic groups for either acceptance of amniocentesis or legal termination of pregnancy (TOP). In the study, the overall acceptance rate of amniocentesis was 75·9% and of TOP in women offered the procedure, 76·3% (D Viljoen, personal communication).

The situation is, however, further complicated by the medical fraternity's lack of awareness of DS in the African population. This is illustrated by the fact that in Johannesburg in 1990, only 5% of amniocenteses were undertaken on African women (who comprised 90% of expectant mothers), and that not one of 34 mothers of DS infants who were of AMA and seen by a medical practitioner in the first trimester, was referred for prenatal counselling and amniocentesis.[9]

Mgone[17] noted that 50% of the mothers in his study considered the raising of their DS infants and children to be a burden. This was also the finding of Kromberg and Zwane[18] who documented that African mothers of DS infants experienced similar stress and responses to being informed of the diagnosis as their First World white counterparts.

Discussion

DS in Africa south of the Sahara has been, and remains to the present, a largely unrecognised problem. This would appear to be because of a lack of clinical awareness of the problem among medical and nursing staff, difficulties in deriving a clinical diagnosis of DS in African neonates, a suspected high infant mortality of affected persons resulting in a low prevalence of DS, and thus a concomitant, limited awareness of the problem in the community. Although this would appear to have only negative connotations for the pre- and postnatal management of DS, from reviewing published reports, the author would suggest that this situation is not dissimilar to that experienced in the First World in the precytogenetic era.[16]

In 1953 Øster, as quoted by Mikkelsen *et al*,[15] could claim that the incidence of DS in Denmark could be reduced to half if mothers over 35 years of age stopped reproducing. The same claim can at present be made for Africa. However, the road forwards for Africa, from that statement to the situation where only two DS children were born to women of AMA in Denmark in 1985,[15] will, owing to the existing Third World African circumstances, be far more tortuous. It will require extensive and appropriate education of medical and nursing staff and the general public. Initially, the prevention of DS will be reliant on social upliftment, public and especially maternal education on DS, and appropriate family planning for women of AMA. Together these could ensure a reduction of mean maternal age with the parallel reduction in DS incidence as experienced in developed countries.[15] Prenatal diagnosis and selective TOP is at present limited to major centres in South Africa, and to the author's knowledge only a few other centres in Africa. Available information from South Africa suggests that, given the correct circumstances as evidenced by the experience in Cape Town and the author's experience in Pretoria, African women in this country would use such facilities appropriately. The challenge for the future is, therefore, the provision of an accessible and cost effective prenatal diagnostic service capable of serving all people, but especially those distant from major centres.

Postnatal management of African DS infants and children will require an innovative approach to overcome the limited facilities available. High mortality from congenital heart disease, exacerbated by infection and malnutrition, can be expected to continue. For those DS children that survive, care and education will have to be obtained from community based programmes for the disabled.

In conclusion, despite the apparent impediments to the management of DS in Africa, this may be the ideal condition with which the concepts of genetic diseases, prenatal diagnosis and management, and postnatal management of the intellectually disabled could be introduced into our Third World situation. This will, however, require extensive and relevant medical and public education and the development of systems of management appropriate for Africa.

1 Stoll C, Alembik Y, Dott B, Roth MP. Epidemiology of Down syndrome in 118 265 consecutive births. *Am J Med Genet (Suppl)* 1990;7:79–83.

2 Down JL. Observations on an ethnic classification of idiots. *London Hospital Clinical Lectures and Reports* 1866;3:259–62.

3 Luder J, Musoke LK. Mongolism in Africans. *Arch Dis Child* 1955;30:310–15.

4 Jelliffe DB. Mongolism in Jamaican children. *West Indian Med J* 1954;3:164–5.

5 Pueschel SM, Steinberg L. *Down syndrome: a comprehensive bibliography.* New York: Garland STPM Press, 1980.

6 Adeyokunno AA. The incidence of Down syndrome in Nigeria. *J Med Genet* 1982;19:277–9.

7 Delport SD, Christianson AL, van den Berg HJS, Wolmarans L, Gericke GS. Descriptive profile of congenital anomalies in black South African neonates born in an urban hospital. *S Afr Med J* 1995;85:15–20.

8 Venter PA, Christianson AL, Hutamo CM, Makhura MP, Gericke GS. Congenital anomalies in rural black South African neonates – a silent epidemic? *S Afr Med J* 1995; 85:11–15.

9 Kromberg JGR, Christianson AL, Duthie-Nurse G, Zwane E, Jenkins T. Down syndrome in the black population. *S Afr Med J* 1992;81:337.

10 Stevenson AC, Johnson HA, Stewart MIP, Golding DR. Congenital malformations: a report of a series of consecutive births in 24 centres. *Bull WHO* 1966;34(suppl): 1–127.

11 Christianson AL, Kromberg JGR, Viljoen E. The clinical features of black African neonates with Down syndrome. *E Afr Med J* 1995;72:306–10.

12 Mgone CS. Physical features in African children with Down's syndrome. *E Afr Med J* 1983;60:314–18.

13 Kromberg JGR, Zwane E, Duthie-Nurse G, Jenkins T. Down syndrome in a third world community. Proceedings of the 8th International Congress of Human Genetics. *Am J Hum Genet Suppl* 1991:49:4A.

14 Hall B. Mongolism in newborns. *Acta Paediatr Scand* 1964; 154:1–95.

15 Mikkelsen M, Poulsen H, Nielsen KG. Incidence, survival and mortality in Down syndrome in Denmark. *Am J Med Genet (Suppl)* 1990;7:75–8.

16 Christianson AL, Kromberg JGR. Maternal non-recognition of Down syndrome in black South African infants. *Clin Genet* (in press).

17 Mgone CS. Reproductive behaviour and attitudes of African mothers following a birth of a Down's syndrome child. *E Afr Med J* 1982;59:555–9.

18 Kromberg JGR, Zwane E. Down syndrome in the black population in the Southern Transvaal. *Southern Afr J Child Adol Psychiatr* 1993;5:30–3.